IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Erik H.F. Wong et al. Serial No.: 10/669,611 Filed: September 24, 2003 Title: METHOD OF TREATING FIBROMYALGIA AND OTHER SOMATOFORM DISORDERS Group Art Unit: 1614 Examiner: Phyllis G. Spivack Attorney Docket No.: 30744/6248.10	I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via EFS-Web to the U.S. Patent and Trademark Office on **September 8, 2006**. /Sandip H. Patel, Reg. #43848/ Sandip H. Patel (Reg. No. 43,848) Attorney for Applicants

RESPONSE TO OFFICIAL ACTION

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

This paper is being presented in response to the non-final official action dated May 9, 2006, wherein: (**a**) claims 41, 44-51, and 54 are pending; (**b**) claims 41, 44-49, 51 and 54 have been rejected under 35 USC § 102(b) as being anticipated by G.D. Burrows et al., "Antidepressant Efficacy and Tolerability of the Selective Norepinephrine Reuptake Inhibitor Reboxetine: A Review," J. Clin. Psychiatry, Vol. 59, Suppl. 14, 4 pages (1998) (hereinafter the "Burrows publication"); and, (**c**) the pending claims have been rejected under 35 USC § 103(a) as being obvious over B.A. Fallon et al., "The Pharmacotherapy of Hypochondriasis," Psychopharmacology Bulletin, Vol. 32(4), pgs. 607-11 (1996) (hereinafter the "Fallon publication"). The rejections are traversed, and reconsideration and withdrawal of the rejections are respectfully requested in view of the following remarks.

This paper is timely filed as it is accompanied by a petition under 37 CFR § 1.136(a) for an extension of time to file in the first month, and payment of the required extension fee.

A complete listing of the existing claims is not required (or presented herein) because no changes are being made to the claims, no claims are being canceled, and no claims are being added. *See* 37 CFR § 1.121(c).

I. The 35 USC § 102(b) Rejection

Pending claims 41, 44-49, 51 and 54 have been rejected under 35 USC § 102(b) as being anticipated by the Burrows publication. (Pending claim 50 has not been rejected under § 102(b) as being anticipated by the Burrows publication.) Specifically, the action (a) interprets independent claim 41 to encompass a method of treating somatoform disorders; (b) asserts that dysthymia is included among those disorders characterized in the specification as somatoform; (c) asserts that the Burrows publication teaches to treat dysthymia with racemic reboxetine; and, (d) concludes that claim 41 and claims dependent therefrom are anticipated by the Burrows publication:

> Claims 1 [*sic*, Claim 41] is interpreted to be drawn to treatment of fibromyalgia, as well as any one of the somatoform disorders that are exemplified on page 27, lines 13-16, of the specification. Because dysthymia is included among those disorders characterized as "somatoform" in the instant specification, the rejection of record is maintained and presently extended to include claim 51 and new claim 54. The commercial product is racemic reboxetine methanesulphonate and is well established prior art.

The action at p. 3.

The rejection is traversed, and reconsideration and withdrawal of the rejection are respectfully requested in view of the response provided below.

A. Proper Basis for a Section 102(b) Rejection

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). Thus, a determination that a claim is anticipated under 35 USC § 102 involves two analytical steps. First, the U.S. Patent and Trademark Office (PTO) must interpret the claim language, where necessary, to ascertain its meaning and scope. In interpreting the claim language, the PTO is permitted to attribute to the claims only their broadest *reasonable* meaning as understood by persons having ordinary skill in the art, considered in view of the entire disclosure of the specification. *See In re Morris*, 127 F.3d 1048, 1054(Fed. Cir. 1997). Second, the PTO must compare the construed claim to a single prior art reference and set forth factual findings that "each and every limitation is found either expressly or inherently [disclosed] in [that] single prior art reference." *Celeritas Techs. Ltd. v. Rockwell Int'l Corp.*, 150 F.3d 1354, 1360 (Fed. Cir. 1998). Additionally, "[t]he identical invention must be shown in as complete detail as is contained in the patent claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989).

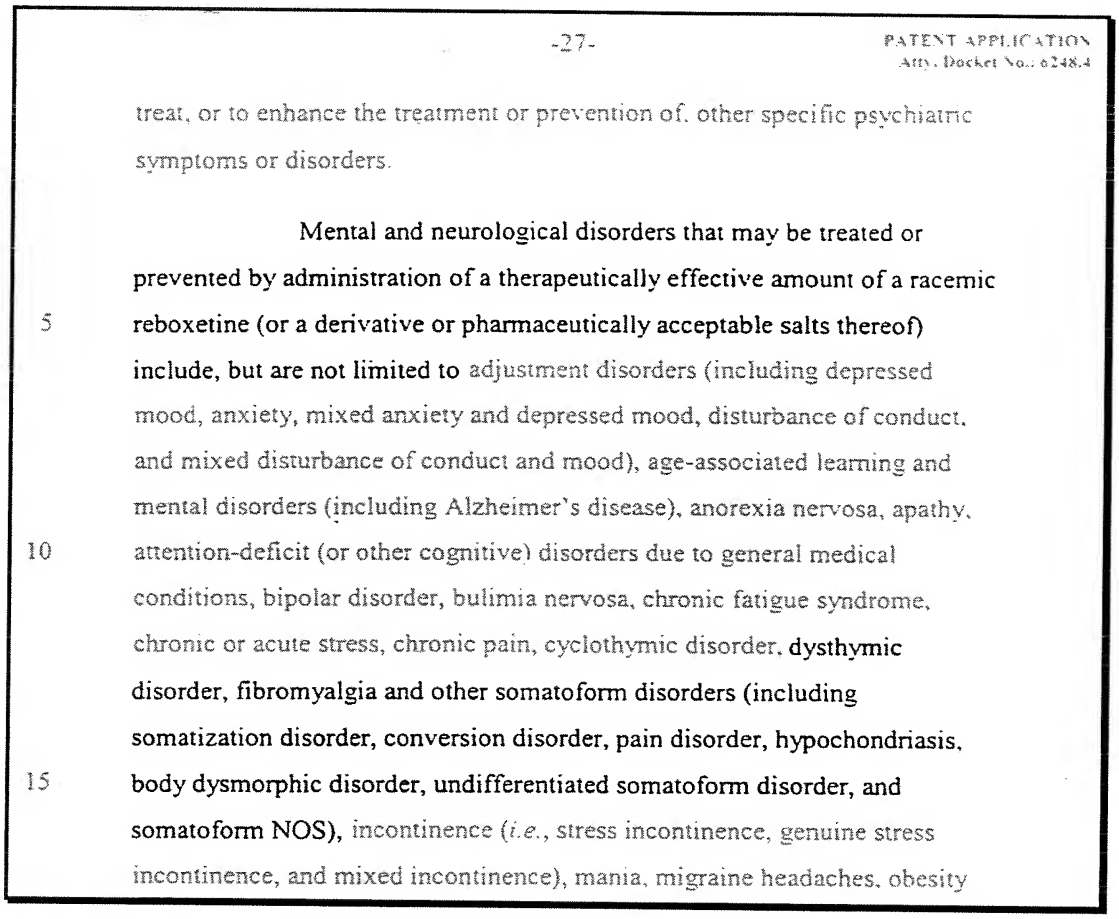
B. The Section 102(b) Rejection Is Traversed

The action misinterprets the pending claims to encompass dysthymia. The pending claims do not recite dysthymia. Furthermore, nothing in the specification suggests that recitations in the claim could encompass dysthymia. To the contrary, the specification makes clear that the pending claims could not encompass dysthymia. Consequently, whether the Burrows publication describes the treatment of dysthymia with racemic reboxetine is not relevant to the section 102(b) analysis of the pending claims. The pending claims are not anticipated by the Burrows publication.

The action's interpretation of claim 41 to encompass a method of treating somatoform disorders is correct. Claim 41 recites a "method of treating an individual suffering from fibromyalgia and other somatoform disorders, the method comprising the step of administering to the individual a therapeutically effective amount of racemic reboxetine or a pharmaceutically acceptable salt thereof." Written description support for this claim can be found in the specification at, for example, page 27, lines 3-16. *See* Figure 1, below. Claim 41 and the other pending claims (which all depend from claim 41), however, do not recite a method for treating dysthymia.

As stated in the applicants' paper filed February 23, 2006, dysthymia is not characterized as a somatoform disorder. Dysthymia is a depressive disorder. In contrast, however, the very essence of somatoform disorders is the presence of somatic symptoms in the absence of identifiable underlying organic pathology. Indeed, somatoform disorders are only diagnosed when psychiatric examination has excluded other mental disorders (including dysthymia). Consequently, there is no basis on which to conclude that dysthymia is a somatoform disorder.

The action's assertion that "dysthymia is included among those disorders characterized as 'somatoform' in the instant specification" is **not** correct. *See* the action at p. 2 (citing p. 27, lines 13-16, of the specification). Contrary to that assertion, the specification **does not** characterize dysthymia as a somatoform disorder. The specification discloses that a "dysthymic disorder" is among the mental and neurological disorders that may be treated by administration of a therapeutically effective amount of racemic reboxetine. However, the specification does not teach or otherwise suggest that a "dysthymic disorder" is, or can be, characterized as a somatoform disorder. Specifically, the specification lists "dysthymic disorder" separately from "fibromyalgia and other somatoform disorders":



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treat, or to enhance the treatment or prevention of, other specific psychiatric symptoms or disorders.

Mental and neurological disorders that may be treated or prevented by administration of a therapeutically effective amount of a racemic reboxetine (or a derivative or pharmaceutically acceptable salts thereof) include, but are not limited to adjustment disorders (including depressed mood, anxiety, mixed anxiety and depressed mood, disturbance of conduct, and mixed disturbance of conduct and mood), age-associated learning and mental disorders (including Alzheimer's disease), anorexia nervosa, apathy, attention-deficit (or other cognitive) disorders due to general medical conditions, bipolar disorder, bulimia nervosa, chronic fatigue syndrome, chronic or acute stress, chronic pain, cyclothymic disorder, dysthymic disorder, fibromyalgia and other somatoform disorders (including somatization disorder, conversion disorder, pain disorder, hypochondriasis, body dysmorphic disorder, undifferentiated somatoform disorder, and somatoform NOS), incontinence (*i.e.*, stress incontinence, genuine stress incontinence, and mixed incontinence), mania, migraine headaches, obesity

Figure 1. Page 27 of the Specification.

That "dysthymic disorder" and "fibromyalgia and other somatoform disorders" are listed in succession does not mean that "dysthymic disorder" is a "somatoform disorder." A more careful review of the list at page 27 will reveal that the list recites disorders alphabetically. Consequently, listing "dysthymic disorder" next to and before "fibromyalgia and other somatoform disorders" is nothing more than the coincidence attendant with an alphabetical list. Furthermore, the specification identifies examples of "other somatoform disorders" in the parenthetical beginning at line 13 and ending at line 16. That parenthetical does not identify dysthymia (or a dysthymic disorder) as a somatoform disorder. *See* Figure 1, above.

The prior official action (dated September 20, 2005) contained a section 102(b) rejection of the claims over the Burrows publication. The applicants' response to that action (filed February 23, 2006) acknowledged that the Burrows publication describes the treatment of dysthymia with racemic reboxetine, completely addressed and traversed the section 102(b) rejection, and argued that there is no scientific support for a position that dysthymia is a somatoform disorder:

> The Burrows publication describes the treatment of major depressive disorder ("MDD") and dysthymia with racemic reboxetine. However, the position set forth in the action (i.e., that "Dysthmia [*sic*, Dysthymia] may be considered a somatoform disorder in that there is no organic basis or known physical cause") lacks any scientific support. Both MDD and dysthymia are forms of **depressive** disorder. It is on this basis that racemic reboxetine—an **established antidepressant**—is effective in the treatment of these conditions. In contrast, however, the very essence of somatoform disorders is the presence of **somatic** symptoms *in the absence of identifiable underlying organic pathology* where the clinician judges that the onset, severity, and duration of somatic symptoms (e.g., pain, gastrointestinal disturbance) are strongly linked to psychological factors.
>
> The diagnostic categories of MDD and dysthymia are distinct nosological entities within the framework of DSM-IV. A diagnosis of dysthymia cannot be subsumed under the heading of somatoform disorders because somatoform disorders are only diagnosed *when psychiatric examination has excluded other mental disorders (including dysthymia).* See, for example, pages 376-77 of DSM-IV, appended hereto for further evidence of the diagnostic feature of dysthymia. The position set forth in the action (i.e., that "Dysthmia [*sic*, Dysthymia] may be considered a somatoform disorder in that there is no organic basis or known physical cause") is not only unsupported by scientific evidence, but also contradicted by scientific evidence.

See p. 13 of the applicants' response filed February 23, 2006 (bold emphases in original, italicized emphases added). These arguments, which are reiterated herein, have gone unaddressed in the current official action.

The action has attributed to the pending claims an unreasonably broad (and incorrect) meaning as understood by persons having ordinary skill in the art, considered in view of the entire disclosure of the specification, in contravention of established legal precedents. *See, e.g., In re Morris*, 127 F.3d at 1054. Had the action properly construed the pending claims and, thereafter, compared the properly construed claims to the Burrows publication, it would have been clear that the Burrows publication does not disclose, either expressly or inherently, each and every element recited in the pending claims. Under the proper claim construction and proper comparison of that construction to the disclosure in the Burrows publication, the Burrows publication does not anticipate the pending claims. *See Verdegaal Bros.*, 814 F.2d at 631; *see also Celeritas Techs.*, 150 F.3d at 1360. Additionally, the Burrows publication does not show the identically claimed invention "in as complete detail as is contained in the" pending claims. *See Richardson*, 868 F.2d at 1236. A disclosure of (**a**) the treatment of dysthymia with racemic reboxetine does not anticipate a claim reciting (**b**) a "method of treating an individual suffering from fibromyalgia and other somatoform

disorders, the method comprising the step of administering to the individual a therapeutically effective amount of racemic reboxetine or a pharmaceutically acceptable salt thereof."

The current action (like the September 20, 2005, action) has not interpreted the language recited in any of the dependent claims (i.e., claims 44-51 and 54) to ascertain the meaning and scope of the language. Furthermore, the current action (like the September 20th action) has not compared the dependent claims to the disclosure in the Burrows publication, and has not set forth any factual findings that the elements recited in these dependent claims are disclosed in the Burrows publication. No meaningful response to the section 102(b) rejection of the dependent claims is possible other than to state that the PTO has not satisfied its burden of demonstrating that the Burrows publication anticipates these claims under section 102(b). As argued above, the Burrows publication does not anticipate independent claim 41. Consequently, the Burrows publication cannot anticipate any claim dependent from claim 41.

Reconsideration and withdrawal of the section 102(b) rejection are respectfully requested in view of the foregoing remarks and those presented in the applicants' paper filed February 23, 2006.

II. The 35 USC § 103(a) Rejection

The pending claims have been rejected under 35 USC § 103(a) as being obvious over the Fallon publication alone. Specifically, the action (a) asserts that the Fallon publication teaches administration of a selective serotonin reuptake inhibitor (fluoxetine) to treat one type of an alleged somatoform disorder; (b) acknowledges that the Fallon publication does not teach administration of reboxetine; (c) asserts that reboxetine is a selective serotonin reuptake inhibitor with almost identical clinical indications as, and a mechanism of action that closely parallels that of, fluoxetine; and, (d) concludes, therefore, that the pending claims are obvious:

> Fallon teaches the administration of the selective serotonin reuptake inhibitor fluoxetine to treat types of hypochondriasis, a somatoform disorder according to DSM-IV. Fibromyalgia is included among somatoform disorders. The claims differ in that Fallon is silent concerning administration of reboxetine. However, reboxetine is a *selective* serotonin reuptake inhibitor with almost identical clinical indications as fluoxetine. Therefore, it would have been reasonable to expect reboxetine to be effective in the treatment of somatoform disorders since its *mechanism of action closely parallels that of fluoxetine*. The determination of optimal dosages, as well as modes of administration, are parameters well within the purview of those skilled in the art through no more than routine experimentation.

See pp. 3-4 of the action (italicized emphases added).

The rejection is traversed, and reconsideration and withdrawal of the rejection are respectfully requested in view of the response provided below.

A. Proper Basis for a Section 103(a) Rejection

The PTO "has the burden under § 103 to establish a prima facie case of obviousness." *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). To establish a prima facie case of obviousness, the PTO must satisfy three basic criteria. First, the PTO must show that the combined disclosure of the prior art references teaches or suggests all of the claim limitations. *See* MPEP § 2143 (8th ed., rev. 3, Aug. 2005). Moreover, it is "incumbent upon the examiner to identify wherein each and every facet of the claimed invention is disclosed in the applied reference." *Ex parte Levy*, 17 USPQ2d 1461, 1462 (Bd. Pat. App. & Inter. 1990).

Second, where obviousness is alleged to arise from a combination of elements across a plurality of references, the PTO must show the existence of some suggestion, motivation, or teaching to those skilled in the art to make the precise combination recited in the claims. *See Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1320 (Fed. Cir. 2004). Compliance with this requirement prevents the PTO's use of "the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability — the essence of hindsight." *Ecolochem, Inc. v. Southern Cal. Edison Co.*, 227 F.3d 1361, 1371-72 (Fed. Cir. 2000) (quoting *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999)). Evidence of a suggestion or motivation to combine prior art references may come from "the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved." *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1125 (Fed. Cir. 2000). The PTO's showing "must be clear and particular, and broad conclusory statements about the teaching of multiple references, standing alone, are not 'evidence.'" *Ibid* (quoting *In re Dembiczak*, 175 F.3d at 1000). Indeed, the U.S. Court of Appeals for the Federal Circuit has consistently held that a person having ordinary skill in the art must not only have had some motivation to combine the prior art teachings, but also some motivation to combine the prior art teachings in the particular manner claimed. *See, e.g., In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000) ("Particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.").

To support a conclusion that a claimed combination is prima facie obvious, either (a) the references must expressly or impliedly suggest the claimed combination to one of ordinary skill in the art, or (b) the PTO must present a convincing line of reasoning as to why a person of ordinary skill in the art would have found the claimed invention to have been obvious in light of the teachings of the references. *See Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985); *see also, In re Rinehart*, 531 F.2d 1048, 1051 (CCPA 1976).

The mere fact that the prior art could be modified as proposed by the PTO is not sufficient to establish a prima facie case of obviousness. *See In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992). The PTO must explain why the prior art would have suggested to one of ordinary skill in the art the desirability of the modification. *Ibid*; *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998) ("In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination.").

Finally, the PTO must demonstrate that a person having ordinary skill in the art would have a reasonable expectation of success when combining the disclosures of the references. The suggestion or motivation to make the claimed invention and the reasonable expectation of success must both be found in the prior art, and must not be derived by hindsight from knowledge of the application's disclosure. *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988); MPEP § 2143.

B. The Section 103(a) Rejection Is Traversed

The PTO has not established a prima facie case demonstrating the pending claims are rendered obvious by the Fallon publication (alone) or even in view of knowledge possessed by a person having ordinary skill in the art. Not only does the Fallon publication fail to disclose all of the features recited in the pending claims (as acknowledged by the action), but, as argued below, the Fallon publication also does not teach, suggest, or motivate the ordinarily skilled artisan to modify the Fallon publication's disclosure to arrive at the claimed invention with a reasonable expectation of success. Furthermore, the ordinarily skilled artisan, having no knowledge of the invention recited in the pending claims, would have not have reasonably concluded from the Fallon publication that he/she may treat an individual suffering from fibromyalgia and other somatoform disorders by administering to the individual a therapeutically effective amount of racemic reboxetine or a pharmaceutically acceptable salt thereof.

1. The Fallon Publication Teaches No Generalizations Regarding SRIs Success in Treating Somatoform Disorders, Like Hypochondriasis

The Fallon publication does not teach or suggest that all serotonin reuptake inhibitors (SRIs) will treat somatoform disorders. The Fallon publication discloses that patients suffering from hypochondriasis—a somatoform disorder listed among those recited in the specification at page 27, lines 13-16 (*see* Figure 1, above)—"responded very well" to the administration of fluoxetine, "responded well" to the administration of clomipramine, and "moderately improved" in response to administration of imipramine. *See* the Fallon publication at p. 608 (col. 2) and 609 (col. 1). Clomipramine, imipramine, and fluoxetine are known SRIs—indeed, fluoxetine is a known *selective* serotonin reuptake inhibitor (SSRI).

Amitriptyline also is a known SRI; however, according to the Fallon publication, hypochondriasis-suffering patients did not respond to the administration of amitriptyline. *See* the Fallon publication at p. 608 (col. 1). Furthermore, desipramine is an active, in vivo metabolite of imipramine; however, according to the Fallon publication, a hypochondriasis-suffering patient did not respond to the administration of desipramine. *See* the Fallon publication at p. 608 (col. 2). Thus, the Fallon publication emphasizes that *selective* serotonin reuptake inhibitors, such as fluoxetine, may provide potential treatment for hypochondriasis, but de-emphasizes that other compounds like SRIs (e.g., amitriptyline, clomipramine and imipramine) and metabolites of SRIs (e.g., desipramine) provide potential treatment for hypochondriasis.

Accordingly, just because the Fallon publication reports that some of the known SRIs elicit favorable responses in hypochondriasis-suffering patients does not, therefore, mean that the skilled artisan would conclude that all known SRIs would elicit such favorable responses. Indeed, a skilled artisan carefully reviewing the Fallon publication—and, for example, that portion of the Fallon publication reporting failed attempts at treating hypochondriasis with amitriptyline—would have reason to doubt that all SRIs would elicit such favorable responses. Consequently, it is not appropriate to generalize that the Fallon publication teaches the ordinarily skilled artisan to administer any SRI to treat an individual suffering from fibromyalgia and other somatoform disorders.

Furthermore, neither the action nor the Fallon publication articulates any basis on which to conclude that compounds other than *selective* serotonin reuptake inhibitors could be useful to treat hypochondriasis-suffering patients. Still further, neither the action nor the Fallon publication articulates any basis on which to conclude that selective norepinephrine reuptake inhibitors—like racemic reboxetine—could be useful to treat hypochondriasis-suffering patients.

2. Pharmacological Similarities among Compounds Are neither Predictive nor Indicative of Success in Treating Hypochondriasis

The Fallon publication does not teach or suggest that all compounds pharmacologically similar to the "effective" SRIs reported therein (i.e., clomipramine, fluoxetine, and imipramine) will treat somatoform disorders. As noted above, the Fallon publication discloses that hypochondriasis-suffering patients responded "very well," "well," and "moderately improved" when administered fluoxetine, clomipramine, and imipramine, respectively. Amitriptyline is a tricyclic compound with known general pharmacological properties similar to those of the structurally related imipramine; however, according to the Fallon publication, hypochondriasis-suffering patients did not respond to the administration of amitriptyline. *See* the Fallon publication at p. 608 (col. 1).

Accordingly, just because the Fallon publication reports that certain antidepressants (i.e., clomipramine, fluoxetine, and imipramine) elicit favorable responses in hypochondriasis-suffering patients does not, therefore, mean that the skilled artisan would conclude that all other antidepressants known to possess pharmacological similarities to these certain antidepressants will treat somatoform disorders. Indeed, a skilled artisan carefully reviewing the Fallon publication—and, for example, that portion of the Fallon publication reporting failed attempts at treating hypochondriasis with amitriptyline, which is pharmacologically similar to imipramine—would have reason to doubt that pharmacologically similar antidepressants would elicit such favorable responses. Consequently, it is not appropriate to generalize that the Fallon publication teaches the ordinarily skilled artisan to administer any compound pharmacologically similar to clomipramine, fluoxetine, and imipramine to treat fibromyalgia and other somatoform disorders.

Furthermore, and as set forth in the specification at page 31, lines 20-22, "racemic reboxetine has an 81 fold selectivity favoring norepinephrine reuptake inhibition over serontonin [sic, serotonin] reuptake inhibition." Racemic reboxetine is, therefore, a selective *norepinephrine* reuptake inhibitor—*not* a selective serotonin reuptake inhibitor. Conclusions in the action that "reboxetine is a selective serotonin reuptake inhibitor with almost identical clinical indications as fluoxetine" and that racemic reboxetine has a "mechanism of action [that] closely parallels that of fluoxetine" are strongly traversed as there is no evidence supporting such conclusions and, to wit, the action identifies no such evidence.

3. The Fallon Publication Expresses Significant Doubts Regarding the Effectiveness of SRIs (Clomipramine and Imipramine) and even SSRIs (Fluoxetine) in Treating Hypochondriasis

The Fallon publication expresses significant doubts, based on its own review, of reports suggesting particular efficacy for the serotonin reuptake inhibitors. The Fallon publication acknowledges that preliminary results obtained in clinical trials administering (to patients suffering from hypochondriasis) fluoxetine versus a placebo do not demonstrate a significant difference between the two, and states that a larger trial is necessary:

> Although these preliminary results do not demonstrate a significant difference between fluoxetine and placebo, the sample size at this analysis was quite small so conclusions must await completion of the larger trial.

Ibid at 610 (col. 1). The Fallon publication concludes that pharmacological trials addressing not only serotonin reuptake inhibitors but also the efficacy of other pharmacologic agents and of specific psychotherapies are needed before reaching any determination that serotonin reuptake inhibitors, as a class, benefit patients suffering from hypochondriasis:

> While serotonin reuptake inhibitors may have a particularly beneficial impact on patients with hypochondriasis,

> conclusions must await the completion of placebo-controlled pharmacologic trials addressing not only serotonin reuptake inhibitors but also the efficacy of other pharmacologic agents and of specify psychotherapies.

Ibid.

The action correctly acknowledges that the Fallon publication **does not** teach or suggest all of the limitations recited in the pending claims. Specifically, the action correctly acknowledges that the Fallon publication does not teach the administration of reboxetine. In fact, the Fallon publication does not teach the administration of reboxetine for any purpose, much less for the purpose of treating fibromyalgia or other somatoform disorders.

The section 103(a) rejection is premised on conclusions that "reboxetine is a selective serotonin reuptake inhibitor with almost identical clinical indications as fluoxetine" and has "a mechanism of action [that] closely parallels that of fluoxetine." *See* pp. 3-4 of the action. The action cites no evidence supporting these conclusions. Without such evidence, there is absolutely no basis on which to conclude the ordinarily skilled artisan would have substituted reboxetine in the place of the Fallon publication's disclosure of the SSRI fluoxetine (or the SRIs clomipramine and imipramine) to treat hypochondriasis. Even if, however, these conclusions were supported by evidence, the Fallon publication still would not have taught the skilled artisan to treat an individual suffering from fibromyalgia and other somatoform disorders by administration of racemic reboxetine or a pharmaceutically acceptable salt thereof. For example, the Fallon publication teaches no generalizations regarding SRIs success in treating somatoform disorders. Furthermore, the Fallon publication does not teach or suggest that all compounds pharmacologically similar to the "effective" SRIs reported therein (i.e., clomipramine, fluoxetine, and imipramine) will treat somatoform disorders.

Not only does the Fallon publication fail to disclose all of the features recited in the pending claims, but the Fallon publication also does not teach, suggest, or motivate the ordinarily skilled artisan to modify the Fallon publication's disclosure to arrive at the claimed invention with reasonable expectations of success. As indicated above, the Fallon publication prevaricates about the response elicited in individuals suffering from hypochondriasis when administered certain SRI compounds (e.g., clomipramine and imipramine) and even the SSRI fluoxetine, and reports that no response indicative of treatment success is elicited when hypochondriasis-suffering patients are administered other SRIs (e.g., amitriptyline) or metabolites of SRIs (e.g., desipramine). The collection of compounds reported in the Fallon publication includes serotonin reuptake inhibitors—some of which elicit favorable responses (e.g., clomipramine, fluoxetine, and imipramine) and others of which elicit no response indicative of treatment (e.g., amitriptyline). The Fallon publication states nothing relative to selective norepinephrine reuptake inhibitors. The Fallon publication concludes that

pharmacological trials addressing not only serotonin reuptake inhibitors but also the efficacy of other pharmacologic agents and of specific psychotherapies are needed before reaching any determination that serotonin reuptake inhibitors as a class benefit patients suffering from hypochondriasis.

Consequently, the ordinarily skilled artisan having reviewed the Fallon publication is not even motivated "to try" other serotonin reuptake inhibitors—still less a selective norepinephrine reuptake inhibitor—to treat hypochondriasis, much less fibromyalgia and other somatoform disorders. At most, the Fallon publication motivates the ordinarily skilled artisan to perform more significant clinical trials with the SSRI fluoxetine. Contrary to the suggestion in the action, the skilled artisan would not have any reasonable expectation that a selective norepinephrine reuptake inhibitor, like racemic reboxetine, would be effective to treat fibromyalgia and other somatoform disorders.

Thus, no prima facie case of obviousness has been made in the instant action, and none exits based on the Fallon publication. Furthermore, given the numerous shortcomings of the Fallon publication, it is respectfully submitted that the claimed invention is unobvious. Accordingly, reconsideration and withdrawal of the section 103(a) rejection are respectfully requested.

Prima facie obviousness under section 103 is a legal conclusion—not a fact. *In re Rinehart*, 531 F.2d at 1052. The foregoing response identifies facts (e.g., evidence in the form of statements in the publications applied by the PTO) rebutting the alleged legal conclusion that the claimed invention is prima facie obvious. All of these facts must be evaluated along with the facts on which the PTO's legal conclusion was originally reached—not the legal conclusion itself. Having requested herein reconsideration of the legal conclusion set forth in the official action, the PTO is obligated to address all of the evidence and base its forthcoming legal conclusion(s) on such evidence, uninfluenced by its earlier conclusions. *Ibid.*

CONCLUSION

In view of the foregoing, reconsideration and withdrawal of the rejections, and allowance of all pending claims 41, 44-51, and 54 are respectfully requested.

Should the examiner wish to discuss the foregoing, or any matter of form or procedure in an effort to advance this application to allowance, the examiner is urged to contact the undersigned attorney.

Respectfully submitted,

MARSHALL, GERSTEIN & BORUN LLP

September 8, 2006

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